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30542	7590	07/14/2006	EXAMINER	
FOLEY & LARDNER LLP			KIM, ALEXANDER D	
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SAN DIEGO, CA 92138-0278			1656	

DATE MAILED: 07/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,833	ARTIS ET AL.	
	Examiner	Art Unit	
	Alexander D. Kim	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 30 May 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-25 is/are pending in the application.
 - 4a) Of the above claim(s) 10-25 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-9 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 03 February 2004 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/15/2004</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input checked="" type="checkbox"/> Other: <u>Notice to Comply</u> . |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (mailed on 05/02/2006), Applicants filed a response received on 05/30/2006. Claims 1-25 are pending in this instant Office action.

Election

2. Applicant's election of Group I, (Claims 1-9) in the reply filed on 05/30/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. 818.03(a)). The requirement is therefore made FINAL.

Claims 1-25 are pending in the instant application. Claims 10-25 are withdrawn from consideration as non-elected inventions. Claims 1-9 will be examined herein.

Priority

3. Applicant's claim for the benefit of an application of prior provisional applications, 06/485,627 filed on 07/07/2003 and 60/444,734 filed on 02/03/2003 under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Information Disclosure Statement

4. The information disclosure statement (IDS) filed on 10/15/2004 has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Compliance with Sequence Rules

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to fully comply with the requirements of 37 C.F.R. 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

The structural coordinates in Table 1 in the instant specification on page 99 teach an amino acid sequence since a particular atom is assigned to a linear amino acid sequence in order. As such, the amino acid sequence disclosed within the atomic coordinates must comply with the sequence rules. Labeling using a SEQ ID No. must be inserted into the brief description of the tables or into the Figure directly.

Tables 1-4 disclose amino acid sequences and/or a nucleic acid sequence must comply with the sequence rules. Labeling using a SEQ ID No. must be inserted into the brief description of the tables or into the Figure directly.

If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID No.

Objections to the Specification

6. The specification is objected to because of the following informalities:
 - a. The specification is objected to because the title is not descriptive of the elected claims. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The examiner suggests the following new title, for example:

---Method of using a Phosphodiesterase 5A (PDE5A) crystal structure for development of ligands---
 - b. The Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases

and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the name of the enzyme (phosphodiesterase 5A) and the source (human kidney) for completeness.

- c. The PDE5A is used for catalytic domain of PDE5. However, the prior art and the instant specification do not provide which residues are considered as the catalytic domain in the instant application. Appropriate clarification is required.
- d. The denominator of equation for Ki disclosed in bottom of pp. 92 is not aligned correctly. Appropriate correction is required.
- e. The specification is objected to for not being in the appropriate format/titled sections required by MPEP §600. The "Brief Description of the Drawings" section, on pages 23, should be prior to the "Summary" section on page 9. For an appropriate amendment of this sort, the text must be added in one amendment and deleted in another amendment. Appropriate correction is required.
- f. The specification is objected for the disclosure interchangeable use of terms "comprising", "consisting essentially of" and "consisting" in the instant application pp. 97, § 0342. However, this definition is repugnant to the art where

the MPEP § 2111.03 clearly define the scope of each of these terms.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-9 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The use of terms "comprising", "consisting essentially of" and "consisting" can be used interchangeably by the instant specification pp. 97, § 0342. This implies claims with said three terms have the exact same scope of claims. However, this definition is repugnant to the art where the MPEP § 2111.03 clearly define the scope of each of these terms. The use of these terms as disclosed in the specification is unacceptable. Appropriate correction is required.

8. Claims 1-3 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the limitation "co-crystals" and the instant specification defines it as non-covalent complex of a ligand and a target molecule in "a crystal form appropriate for analysis by X-ray or protein crystallography" (see pp. 15, lines 5-6 in § 0038). However, the instant claim is a method of developing

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ligands and determining the orientation of a molecule required to use the three-dimensional coordinate representing the structure of PDE5A-ligand complex.

Moreover, the identification of a molecular scaffolds and modification may alter the binding affinity or specificity because the modeling of molecule in simulation is not an actual physical phenomenon.

After synthesis of a ligand, the method claim is missing a critical method steps to achieve claimed inventions (i.e. screening, assaying to identify a ligand). Alternatively, the preamble can be added into the claims, ---A method for developing ligands with altered binding affinity and/or specificity---, for example. Clarification is required.

9. Claims 2 and 7 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2 and 7 recite the limitation "weak binding compound" and "binds weakly", respectively. However, the term "weak" or "weakly" is a relative term which renders the claim indefinite. The term "weak" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Clarification is required.

10. Claims 4-9 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 recite the limitation "derivative". The term

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"derivative" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear how similar the derivative must be to the initial compound. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-3 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to a method for developing ligands binding to PDE5A by determining the orientation of scaffolds; modifying scaffolds and synthesizing modified scaffolds.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants

must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical Inc. v. Gen-Probe Inc.* (CAFC (2002) 63 USPQ2d 1609).

University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v. G.D. Searle & Co.* the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description as noted from *Enzo Biochemical* (see above).

The instant specification teaches a method for developing ligands to PDE5A using the three-dimensional coordinate of PDE5A disclosed in the Table 1. However, the breath of claims includes a method for developing ligands by any possible PDE5A co-crystal structure coordinate. The instant specification teaches only one species of method for developing ligands using the coordinates of Table 1. The prior art also teaches one species of method for developing ligands using the coordinates of *Saccharomyces cerevisiae* YKG9 protein as disclosed by Ho et al. (2000). However,

the specification and the prior art do not teach sufficient correlations between a structure of PDE5A co-crystal and a function of binding site residues. Because the lack of correlation between structure and function and the claimed genus cannot be represented by the disclosure of instant specification, one skilled in the art would not be in possession of the claimed genus inventions by the instant specification.

12. Claims 5-6 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to a method for developing ligands specific for PDE5A with an affinity at least 10-fold greater than any other PDEs.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure

of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical Inc. v. Gen-Probe Inc.* (CAFC (2002) 63 USPQ2d 1609).

University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v. G.D. Searle & Co.* the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description as noted from *Enzo Biochemical* (see above).

The instant specification teaches a method for developing ligands specific for PDE5A. However, the breath of claims includes a method for developing all compounds having 10-fold greater specificity toward PDE5A compared to other PDE. The instant specification teaches several species of compounds in pp. 93 without disclosing any assay results. The prior art teaches a method of developing ligands by disclosing an inhibitor compound Zaprinast, for example, in pp. 4718 Table 1 of Rascon et al. (2002), which has more than 10 fold greater specificity toward PDE5 compared to TbPDE2B. Therefore, the specification and prior art do not teach sufficient correlations between a structure of compounds and function of having greater than 10 fold

specificity. Because the lack of correlation between structure and function, and the claimed genus cannot be represented by the disclosure of instant specification, one skilled in the art would not be in possession of the claimed genus inventions by the instant specification.

13. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for a method for developing a ligands binding to PDE5A by a three-dimensional coordinates of Table 1, however, does not reasonably provide enablement for a method for developing ligands binding to PDE5A by any other three-dimensional coordinates representing all possible conformational variation of PDE5A.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of

experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The nature of invention is drawn to a method for developing ligands binding to PDE5A by any three-dimensional coordinate of PDE5A-ligand co-crystals. The breadth of Claims 1-3 is broad as to encompass a method of using any possible PDE5A co-crystal structure. However, the specification and prior art do not disclose sufficient working examples for enablement of genus method. The specification provides only one working example of a method using PDE5A coordinates provided by the Table 1. The prior art also discloses one working example of a method for developing ligands binding to PDE5A by Ho et al. (2000). Because the direction and guidance are insufficient, making ligands binding to PDE5A is unpredictable by a claimed genus method. By all the reasons above, the quantity of experimentation needed to make or use the invention claimed based on the content of the disclosure is very high thus requiring undue experimentation for a skilled artisan to make and use the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-9 rejected under 35 U.S.C. 102(b) as being anticipated by Ho et al. (The EMBO Journal (2000) vol. 19(20), pp. 5288-5299). The instant claim is drawn to a method for developing ligands binding to PDE5A by identifying one or more molecular scaffolds that bind to a PDE5A, determining the orientation of molecular scaffolds in co-crystal with PDE5A, identifying chemical structure and synthesizing a ligand with altered binding affinity/specification.

Ho et al. teach a method of developing ligands by disclosing a co-crystal structure model of cyclic-GMP(cGMP)-PDE5-GAF_a motif in Fig. 7A and close up view of cGMP binding site of the PDE5 in Fig. 7B (see pp. 5295 left column). Ho et al. also disclose three previously known active site residues are "located on conserved core structures and can therefore be pinpointed reliably in the modeled structure of PDE5-GAF_a" (see pp. 5293, bottom of left column). The cGMP in the co-crystal structure of Ho et al. was "manually docked" (see description of Fib. 7(b)) thus serve as molecular scaffold for PDE5A. Ho et al. also disclose "PDE5 and PDE6 are highly specific for cGMP as substrate, while PDE2 hydrolyzes both cAMP and cGMP" thus disclosing a modified molecular scaffold, which is cAMP, having altered affinity and/or binding specificity as disclosed in the instant claims. The molecular scaffolds cGMP of Ho et al. binds to a plurality of phosphodiesterase PDE 5, 6 and 11 (see middle of right column, pp. 5288). The instant specification defines the term "binds" (pp. 11 §0024) as "interaction between a target and a potential binding compound" and have preferably "a

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dissociation constant (k_d) of 1 mM or less". Ho et al. teach the "GAF domain of phosphodiesterase 5 binds with $K_d=650$ nM" with cGMP (see Abstract). Ho et al. also teach a method of developing compounds from a molecular scaffold (i.e. cGMP or cAMP), which interact with several key active site residues by identifying active site residues (see Fig. 7(B) and brief description, pp 5295). Thus Ho et al. teach all the claim limitations as disclosed in Claims 1-9.

15. Claims 4-9 rejected under 35 U.S.C. 102(a) as being anticipated by Rascon et al. (PNAS (2002) Vol. 99(7), pp. 4714-4719) as evidenced by Turko et al. (Mol Pharmacol (1999) Vol. 56, pp. 124-130). The instant claim is drawn to a method for developing ligands specific for PDE5A by identifying compounds with plurality and a derivative with greater specificity for PDE5A.

Rascon et al. teach a method of developing ligands by assaying PDE activities in the presence of inhibitors and each inhibition was analyzed in Table 1. Rascon et al. teach using Zaprinast which has IC₅₀ of 0.76 uM and >50 toward PDE5 and Tb PDE2B, respectively. The Sildenafil (a derivative) is assayed to have an IC₅₀ of 0.0039 uM and >100 toward PDE5A and Tb PDE2B thus compounds of Rascon et al. meets the limitation of having at least 10-fold greater specificity for PDE5A. Zaprinast also binds to PDE6 with IC₅₀ of 0.15 uM thus meets the claim limitation of plurality (see Table 1, pp. 4718). Rascon et al. also teach the active site GAF domain of TbPDE2B "are very similar to the two GAF domains found in mammalian PDE2, PDE5, PDE6, PDE10, and PDE11" (see middle of left column, pp. 4718) therefore Zaprinast would also interact

with the active site of PDE11 as inhibitor. Zaprinast interacts with at least one conserved PDE5A active site residues because it is competitive inhibitor as evidenced by Turko et al. (see Abstract, left column). Turko et al. also teach a site-directed mutagenesis to "examine the contribution of 23 conserved amino acids in the catalytic domain of PDE5" "by the classic PDE5 inhibitor zaprinast" (see top left column, pp. 125) and the results are shown in Table 1 in page 129. Thus Rascon et al. teach all limitations of Claims 4-8.

Additional References

16. The following are cited to complete the record but is not prior art:

- a) Sopory et al. (2003) FEBS Letters, *Modeling and mutational analysis of the GAF domain of the cGMP-binding, cGMP-specific phosphodiesterase, PDE5.*, Vol. 539, pp. 161-166.
- b) Card et al. (2004) Structure, *Structural Basis for the Activity of Drugs that Inhibit Phosphodiesterases.*, Vol. 12, pp. 2233-2247.
- c) Erguden et al. (PCT Pub. Date: Jan. 3, 2003) PCT/EP02/06322, Imidazotriazines for use as phosphodiesterase inhibitors. Now US Pat. 6,936609.
- d) Whitehead et al. (USPAT 6,479,493, Nov. 12, 2002,) Methods for treatment of type I diabetes., cites "medical therapy that involves the administration of the PDE2 inhibitor (preferably also a PDE5 inhibitor)" see column 41, bottom of left and Claims 1-3.
- e) Earle et al. (USPAT 6,465,494, Oct. 15, 2002) Methods for treatment of cystic fibrosis., cites Compound 38, a PDE2/5 inhibitor, and a method using PDE5 inhibition (see top of column 38 and Claims 2-3).

Conclusion

17. Claims 1-9 are rejected for the reasons identified in the numbered sections of the Office Action. Applicants must respond to the objections/rejections in each of the numbered sections in the Office action to be fully responsive in prosecution. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 8AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alexander Kim
July 10, 2006



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SUPERVISORY PATENT EXAMINER